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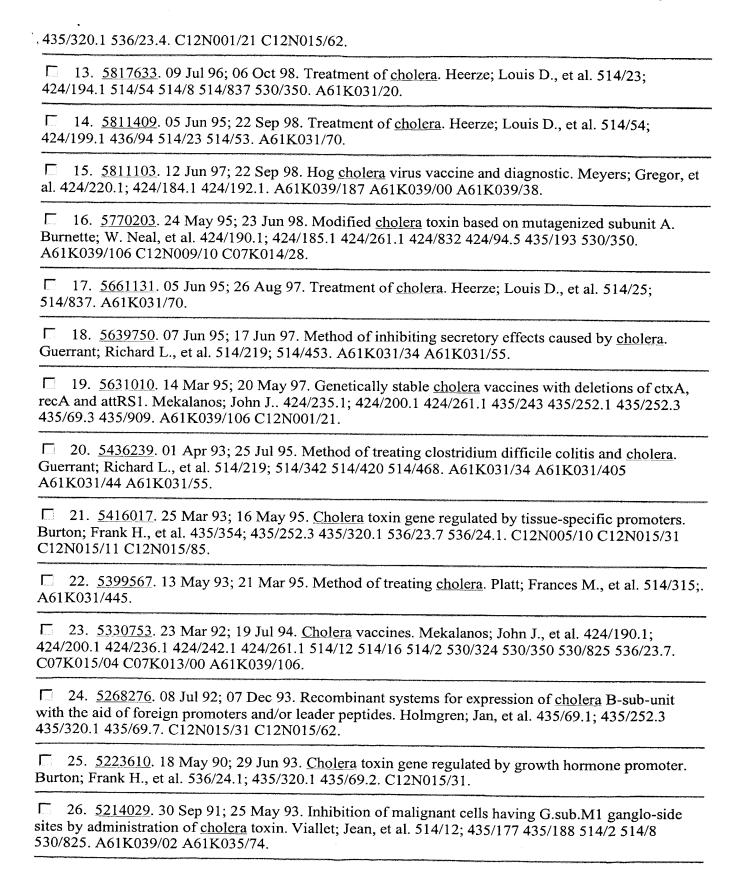
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L1: Entry 1 of 59

File: USPT

Nov 21, 2000

US-PAT-NO: 6149919

DOCUMENT-IDENTIFIER: US 6149919 A

TITLE: Immunogenic detoxified mutants of <a href="cholera">cholera</a> toxin and of the toxin LT, their preparation and their use for the preparation of vaccines

DATE-ISSUED: November 21, 2000

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY Domenighini; Mario Quercegrossa IT Rappuoli; Rino Quercegrossa ITPizza; Mariagrazia Siena IT Hol; Wim Seattle WA

ASSIGNEE-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY TYPE CODE Biocine S.p.A. Siena IT 03

APPL-NO: 08/ 823120 [PALM]
DATE FILED: March 25, 1997

## PARENT-CASE:

This application is a continuation of application Ser. No. 08/256,003, filed Nov. 11, 1994, which is a filing under 35 U.S.C. 371 of PCT/EP92/03016, filed Dec. 30, 1992 abandoned; and which is a filing from parent Italian patent application M191 A 003513, filed Dec. 31, 1991.

FOREIGN-APPL-PRIORITY-DATA:

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US-CL-ISSUED: 424/236.1; 424/184.1, 424/234.1, 424/240.1, 424/241.1, 424/257.1, 424/261.1, 435/69.3, 435/172.3
US-CL-CURRENT: 424/236.1; 424/184.1, 424/234.1, 424/240.1, 424/241.1, 424/257.1, 424/261.1, 435/69.3

FIELD-OF-SEARCH: 424/240.1, 424/241.1, 424/257.1, 424/261.1, 424/184.1, 424/234.1, 424/236.1, 435/69.3, 435/172.3

PRIOR-ART-DISCLOSED:

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Search Selected Search ALL Clear

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ART-UNIT: 161

PRIMARY-EXAMINER: Housel; James C.

ASSISTANT-EXAMINER: Portner; Virginia

ATTY-AGENT-FIRM: Trujillo; Doreen Y. Harbin; Alisa A. Blackburn; Robert P.

### ABSTRACT:

An immunogenic detoxified protein comprising the amino acid sequence of subunit A of of cholera toxin (CT-A) or subunit A of an Escherichia coli heat labile toxin (LT-A) A) or a fragment thereof wherein one or more amino acids at, or in positions corresponding to Val-53, Ser-63, Val-97, Tyr-104 or Pro-106 are replaced with another amino acid or deleted. Examples of specific replacements include Val-53-Asp, Asp, Val-53-Glu, Val-53-Tyr, Ser-63-Lys, Val-97-Lys, Val-97-Tyr, Tyr-104-Lys, Tyr-104-Asp, Tyr-104-Ser, Pro-106-Ser. The immunogenic detoxified protein is useful as vaccine for Vibrio cholerae or an enterotoxigenic strain of Escherichia coli and is produced by recombinant DNA means by site-directed mutagenesis.

9 Claims, 4 Drawing figures

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